Neuroendocrine Breast Carcinoma: Case Report and Review of the Literature

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Keywords

Breast cancer · Neuroendocrine carcinoma · Nuclear scan · Oncology · Pathology · Radiology

Abstract

Primary breast carcinoma with neuroendocrine features is an uncommon presentation of mammary cancers. The authors present a case of a rapidly growing breast mass that raised many differential diagnoses. The diagnosis in this case was challenging. Extensive clinical assessment, radiological imaging, nuclear scans, pathological evaluations, and series of multidisciplinary meetings were utilized to reach the diagnosis of neuroendocrine breast carcinoma.

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Introduction

The reported incidence of the rare neuroendocrine breast tumors comprises 2–5% of all breast carcinomas. The diagnosis depends mainly on the radiologically and histopathologically detected criteria [1, 2]. The World Health Organization categorized these tumors as a subtype of invasive breast cancer based on endocrine features [3].

The clinical and radiological features may not differ from other invasive cancers; however, the diagnosis is solely made on the discovery features similar to neuroendocrine tumors arising from the gastrointestinal tract or lungs. These tend to express neuroendocrine markers in >50% of cases [4].

Case Report

A 40-year-old Asian female, a mother of 3 children (14 years, 7 years, and 10 months old), resident of the same area for the past 8 years, while lactating she noticed a rapidly growing left mass of 2-month duration. There were no associated pain, discharge, skin changes, or systemic manifestations. Gynecological history was unremarkable with regular menstrual cycles and intermittent use of oral contraceptive pills. There was no family history of breast cancer or similar a presentation.

General Examination Was Unremarkable

Local examination revealed breast asymmetry, with a 4-fold increase in the left breast size. A 10 × 12-cm mass occupied both lower and lateral quadrants extending from 2 and 7 o'clock. The overlying skin was stretched and edematous, with areas of peau d'orange. Nipple and

the areola complex were stretched but uncompromised. A large 3 × 3-cm solitary, mobile nontender lymph node was palpated in the ipsilateral axilla (Fig. 1).

The primary clinical impression was locally advanced breast cancer. Initial standard investigations included ultrasound (Fig. 2) and mammogram (Fig. 3a, b), followed by FNAC and core needle biopsy. Cytology was reported as positive for malignant cells. Core biopsy showed an undifferentiated malignant neoplasm with markedly

atypical, hyperchromatic, pleomorphic cells with abundant mitosis and apoptosis. Scattered foci of necrosis were also evident (Fig. 4a, b).

Computed tomography and nuclear bone scans both demonstrated the breast lesion with no evidence of distal metastasis (Fig. 5). Technetium-99m-octreotide scan confirmed isotope uptake in both the left breast mass and the ipsilateral axillary node consistent with positive somatostatin receptor lesions (Fig. 6a, b).

Fig. 1. Clinical appearance at presentation with obvious asymmetry and overstretched overlying skin and edema of the left breast.

Fig. 2. Ultrasound: large lobulated heterogeneous hypoechoic mass occupying the left lateral breast; gray scale and shear wave elastography demonstrated the mass with peripheral blue ring on elastography, highly suspicious of malignancy.

Fig. 3. a, b Mammography of the left breast: CC and MLO views demonstrate a partially circumscribed hyperdense mass with overlying skin thickening, highly suspicious for malignancy, BI-RADS 4C.

Fig. 4. a, b 5× and 10× microscopic picture demonstrating tumor invading the nearby breast parenchyma as obtained from the core biopsy.

Fig. 5. Tc-99m HDP bone scan. Anterior and posterior views. Heterogeneous soft tissue tracer uptake noted within the left breast correlating to the extensive primary left breast mass. There is no scintigraphic evidence of any obvious sinister osseous lesions in this study.

Mastectomy with axillary dissection was the consensus based on the lengthy discussion of the multidisciplinary meeting. Intraoperatively, the large firm mass was found to be firmly attached to the overlying stretched, edematous skin with no adherence to deep fascia (Fig. 7a, b).

The mastectomy specimen weighed 700 g, measuring 19 × 9 × 13 cm. The mass appeared well circumscribed and gray to white in color with areas of hemorrhage and necrosis. A number of matted axillary lymph nodes were recovered and the largest measured 4.4 × 2 cm (Fig. 7c, d).

Microscopic examination of the mass revealed malignant cells arranged in diffuse pattern with focal rosette formation and prominent vascularity. The cells showed cellular and nuclear pleomorphism, finely granular, salt and pepper chromatin, scattered apoptosis, and extensive necrosis (Fig. 8).

A large panel of immunohistochemical analysis was performed which included Pan-CK, CK5/6, CK-7, CK8/18, HMW-CK, E-cadherin, Mammaglobin, GCD-FP-63, ER, PR, Her2/neu, vimentin, myeloperoxidase, CD-34, LCA, CD-68, PLAP, HMB-45, and chromogranin.

They were all reported as negative. Ki67 was reported of 95%. And, immunocytochemical analysis of S100, CD56, and synaptophysin were reported as positive (Fig. 9).

Based on the cumulative data obtained from the clinical features, radiological images, nuclear uptake, morphological appearance, and the immunocytochemical markers, the final diagnosis of “poorly differentiated invasive neuroendocrine carcinoma” was reached. The patient had an uneventful postoperative course and was discharged in a good condition to be followed in an outpatient multidisciplinary clinic. At 6 months, the patient remains in good condition with no evidence of local recurrence.

Discussion

Thorough clinical evaluation, extensive radiological imaging coupled by nuclear scans and comprehensive pathological immunocytochemical analysis maybe required to reach the uncommon diagnosis of primary neuroendocrine breast carcinoma. The value of multidisci-

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Fig. 6. Octreotide scan SPECT-CT: avid uptake at left breast mass and ipsilateral axillary lymph node with no other octreotide avid-detected lesions.

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Fig. 7. The skin marking prior to the mastectomy (a), preserving as much as possible of normal skin (b), the firm specimen (c), and matted axillary nodes (d).

Fig. 8. 20× microscopic picture showing the tumor with prominent vascularity, many mitosis, and cell apoptosis.

Fig. 9. 20× microscopy showing tumor cells positive for CD56.

plinary team collaboration is of fundamental importance in the management of such cases [3].

Secondaries to the breast should be both radiologically and pathologically excluded prior to committing to the diagnosis of primary mammary carcinoma. Neuroendocrine tumors of the breast occur predominately in postmenopausal women; however, it has also been reported in younger patients.

Neuroendocrine tumors commonly originate from the gastrointestinal tract, pancreas, and lungs. The subclassification ranges from well-differentiated to poorly differentiated tumors.

Poorly differentiated neuroendocrine tumors morphologically resemble small cell carcinoma of the lung. Some invasive breast cancer may acquire neuroendocrine morphology features with positive markers [5].

Thirty percent of invasive breast carcinomas can express neuroendocrine differentiation specifically in mucinous and solid papillary carcinomas. The expression of the neuroendocrine markers synaptophysin or chromogranin is essential to confirm the diagnosis [6]. Many theories have suggested that neuroendocrine tumors arise from deviating differentiation of malignant cells with no preexisting neuroendocrine stem cells [7–9]. It is interesting to note that benign neuroendocrine tumors are not known to occur in the breast [10, 11].

Primary neuroendocrine carcinoma of the breast depicts distinct mammographic features that may differ from those of invasive mammary carcinoma. It may appear round, oval, well circumscribed, or lobulated masses that are usually categorized radiologically as BIRAD 4 [12].

PET/CT, CT scan, MRI, and endoscopy maybe helpful tools in aiding diagnosis [13]. The use of somatostatin receptor imaging maybe be of importance in accuracy of follow-up. Its reported sensitivity, specificity, accuracy, positive predictive value, and negative predictive value of Tc-99m-OCT scan were 96, 100, 97, 100, and 94%, respectively [14].

Despite the reported poor outcomes, the standard management plan is no different from invasive breast cancer. Similar guidelines apply to the surgical options being breast-conserving surgery or mastectomy [15–17]. Adjuvant treatment regimens are generally based on immunohistochemistry.

Endocrine therapies may have an advantage in susceptible tumors. Somatostatin analogs are suggested for tumors with somatostatin receptor expression [18, 19]. The diagnosis of primary *poorly differentiated invasive neuroendocrine carcinoma* is an uncommon challenging entity that requires diligent multimodality management.

Statement of Ethics

The authors hereby state that the patient has given her signed written informed consent through her guardian (husband), granting permission for all the materials used in the diagnosis and management to be published in a medical journal.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

All authors contributed actively to this manuscript. The following list delineates the contribution of each author: (1) Maha Abdel Hadi (first author): case selection and designed and reviewed the manuscript, (2) Nosieba Telmisani: provision of the clinical account and literature review, (3) Afnan Al Muhanna: provision of images and radiological diagnosis, (4) Ayesha Ahmed: provision of histopathology slides and interpretation, (5) Haitham Kussaibi: provision of histopathology slides and interpretation, (6) Mohammed Iftikhar: provision of clinical account and literature review, (7) Mohammad Nizami: provision of nuclear images and diagnosis, and (8) Arwa Nabhan: participation in clinical diagnosis and management plan.

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